PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 122635	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. PCT/NZ2003/000194	International Filing Date *(day/month/year)* 1 September 2003	Priority Date *(day/month/year)* 1 September 2002
International Patent Classification (IPC) or national classification and IPC Int. Cl. [7] B01J 8/06, 19/30		
Applicant THE UNIVERSITY OF WAIKATO et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheet(s).

3. This report contains indications relating to the following items:

   - I [X] Basis of the report
   - II [ ] Priority
   - III [ ] Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV [ ] Lack of unity of invention
   - V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI [ ] Certain documents cited
   - VII [ ] Certain defects in the international application
   - VIII [ ] Certain observations on the international application

Date of submission of the demand 28 June 2004	Date of completion of the report 20 October 2004
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer GEORGE CARTER Telephone No. (02) 6283 2154

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/NZ2003/000194

I. Basis of the report

With regard to the elements of the international application:*

☐ the international application as originally filed.

☒ the description, pages 1-6, 8-23 as originally filed,
pages , filed with the demand,
page 7 received on 14 September 2004 with the letter of 14 September 2004

☒ the claims, pages 25-28 as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
page 24 received on 14 September 2004 with the letter of 14 September 2004

☒ the drawings, pages 1-14 as originally filed,
pages , filed with the demand,
pages , received on with the letter of

☐ the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages

☐ the claims, Nos.

☐ the drawings, sheets/fig.

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/NZ2003/000194

V. **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-32	YES
	Claims		NO
Inventive step (IS)	Claims	1-32	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-32	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Novelty, Inventive Step and Industrial Applicability

The present invention is directed to a reaction process which is characterised by a moving reaction phase formed by introducing reaction components having differing flow rates (based on their molecular size) into a medium. The reaction products formed are then separated from the medium. The inventive concept behind the invention lies in the recognition that the reaction and separation can be controlled by controlling various operating parameters that affect the reaction time and progress of the moving reaction zone within the column.

The closest prior art documents are:
WO 2003020411
EP 0142103
US 4259186

However none of these documents discloses a moving reaction zone having a reaction time controlled by controlling the various operating parameters, and therefore claims 1-32 are novel, inventive and are industrially applicable.

limitation on the present invention in any way as other reaction components could include catalysts, which are neither consumed nor altered by the chemical reaction in which it participates; or buffer components, which control pH and thus the moving reaction phase.

In some embodiments the differences in flow rate through the medium will be a consequence of the molecular weight of at least one reaction component.

However, differences in flow rate may be due to other physicochemical characteristics such as electrostatic charge, ligand interaction and so forth. As such, this should not be seen as a limitation on the present invention in any way.

A number of the reaction components may have the same flow rate characteristics, the moving reaction phase being determined by another reaction component with a different flow rate.

The term "moving reaction phase" can be defined as the point where all reaction components necessary for a given reaction are present in the same space in the medium at the same period in time as dictated by the differing flow characteristics of at least some of the reaction components.

The physical and/or chemical properties of the medium which provide differing flow rates to the reaction components naturally leads to separation of the reaction products through the same principles.

The term "medium" can be defined as anything which imparts different flow rates on the basis of a compound's physicochemical properties. The medium may be a chromatographic resin, porous beads, gel, viscous solvent or so forth.

In preferred embodiments of the present invention, the medium will preferably be porous beads, with the moving reaction phase and separation occurring through the

WHAT WE CLAIM IS:

1. A reaction process,

   characterised by the step of

   introducing reaction components to a medium,

   wherein at least one of the reaction components has a different flow rate from the other reaction component(s) through the medium, so that a moving reaction phase is formed which causes reaction products.

2. A reaction process as claimed in claim 1

   characterised by the further step of

   separating the reaction products from the medium.

3. A reaction process as claimed in claim 1 or claim 2 wherein the differences in flow rate through the medium are a consequence of the molecular size of at least one reaction component.

4. A reaction process as claimed in claim 1 or claim 2 wherein the differences in flow rate through the medium are due to electrostatic charge.

5. A reaction process as claimed in claim 1 or claim 2 wherein the differences in flow rate through the medium are due to ligand interaction.

6. A reaction process as claimed in claim 1 wherein the properties of the medium that provide differing flow rates to the reaction components also leads to separation of the reaction products.

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2. A reaction process as claimed in claim 1

characterised by the further step of

separating the reaction products from the medium.

3. A reaction process as claimed in claim 1 or claim 2 wherein the differences in flow rate through the medium are a consequence of the molecular weight of at least one reaction component.

4. A reaction process as claimed in claim 1 or claim 2 wherein the differences in flow rate through the medium are due to electrostatic charge.

5. A reaction process as claimed in claim 1 or claim 2 wherein the differences in flow rate through the medium are due to ligand interaction.

6. A reaction process as claimed in any one of claims 1 to 5 wherein the properties of the medium that provide differing flow rates to the reaction components also leads to separation of the reaction products.

7. A reaction process as claimed in claim 1 wherein the medium includes porous beads.

8. A reaction process as claimed in claim 7 wherein the beads are made of a crossed linked polymeric material.

9. A reaction process as claimed in claim 8 wherein the crossed linked polymeric material includes dextran.

10. A reaction process as claimed in claim 8 wherein the crossed linked polymeric material includes agarose.

11. A reaction process as claimed in claim 1 wherein the moving reaction phase is controlled by altering the properties of the medium.

12. A reaction process as claimed in claim 1 wherein the moving reaction phase is controlled by altering the volumes of the reaction components through the column.

13. A reaction process as claimed in claim 1 wherein the moving reaction phase is controlled by altering the overall flow rate through the column.

14. A reaction process as claimed in claim 1 wherein the reaction products are selectively removed from the reaction zone, preventing them from being involved in subsequent reactions.

15. A reaction process as claimed in claim 14 wherein the reaction products are selectively removed from the reaction zone due to differences in molecular size between the reaction components and the reaction products.

16. A reaction process as claimed in any one of claims 1 to 15 wherein the properties of the medium are selected to substantially prevent particular reaction products from forming.

17. A reaction process as claimed in claim 1 wherein the properties of the medium are selected to orient the reaction components to provide selectivity of an active site in reactions where multiple active sites exist.

18. A reaction process as claimed in claim 1 wherein an active site is protected through the use of protection chemistry to selectively produce a particular reaction product.

19. A reaction process as claimed in claim 1 wherein the reaction process is used for glycosylation reactions.

20. A reaction process as claimed in claim 1 wherein the reaction process is used for polymerisation.

21. A reaction process as claimed in claim 1 wherein the reaction process is used for cleavage reactions.

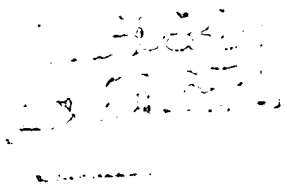
22. A reaction process as claimed in claim 1 wherein the reaction process is used for protein PEGylation.

23. A reaction process as claimed in claim 1 wherein the reaction process is controlled using size-exclusion reaction chromatology.

24. A method of protein PEGylation,

characterised by the step of

forming a moving reaction phase using a reaction process as claimed in claim 1.



25. Reaction products produced by the reaction process as claimed in claim 1.

26. Reaction products as claimed in claim 25 wherein the products are PEGylated protein.

27. Use, in the manufacture of a pharmaceutical composition, of reaction products produced by the reaction process of claim 1.

28. A kitset to bring two or more reaction components together, including

at least two reaction components,

a medium,

characterised in that

at least one of the reaction components has a different flow rate from the other reaction component(s) through the medium, so that a moving reaction phase is formed, which produces reaction products.

29. A kitset for use in a reaction process as claimed in claim 1, including

unit volumes of at least two reaction components,

a medium,

instructions and means for bringing two or more reaction components together in a moving reaction phase.